Diabetes Mellitus: An introduction for persons undergoing organ transplant

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Objectives

1. Introduce diabetes mellitus
2. Understand that diabetes mellitus develops when insulin secretion falls to an extent that normal glucose tolerance is not maintained
3. Discuss rationale to treat diabetes and keep blood glucoses under good control
4. Emphasize importance of 4 components of a treatment regimen

No Conflicts of Interest

What "Diabetes" Means

- Dia (from the Greek δια)= through

Examples:	diarrhea	=	to flow through
	diagonal	=	through an angle
	diaspora	=	to scatter through
	diagnosis	=	to know through
	diameter	=	to measure through
	diaper	=	white throughout

- Betes (from the Greek βαινω)= to pass

Diabetes = to pass through

- Diabetes Mellitus
  - Mellitus: a latin word meaning sweet like honey
  - In English: used in the adjective mellifluous (flowing with sweetness)
- Definitions of Diabetes Mellitus (DM)
  - A group of common metabolic disorders with a shared manifestation of high blood glucose levels (hyperglycemia)
  - Distinct forms of DM result from a complex interaction between genetics and environment
- So, what keeps the blood glucose normal ?

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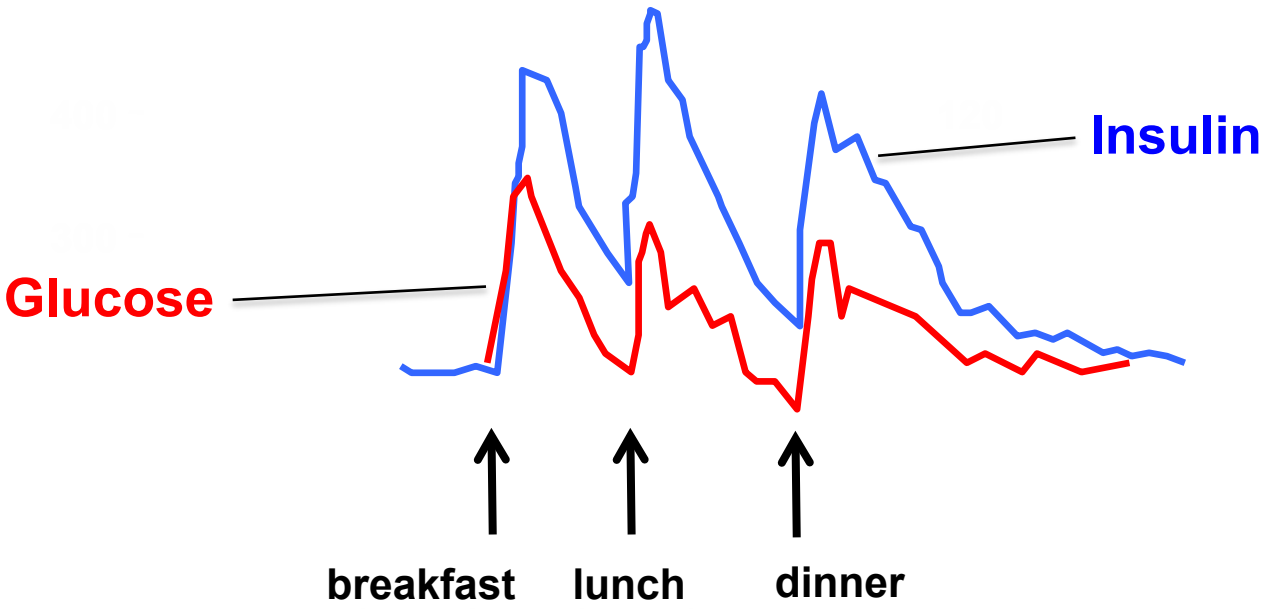
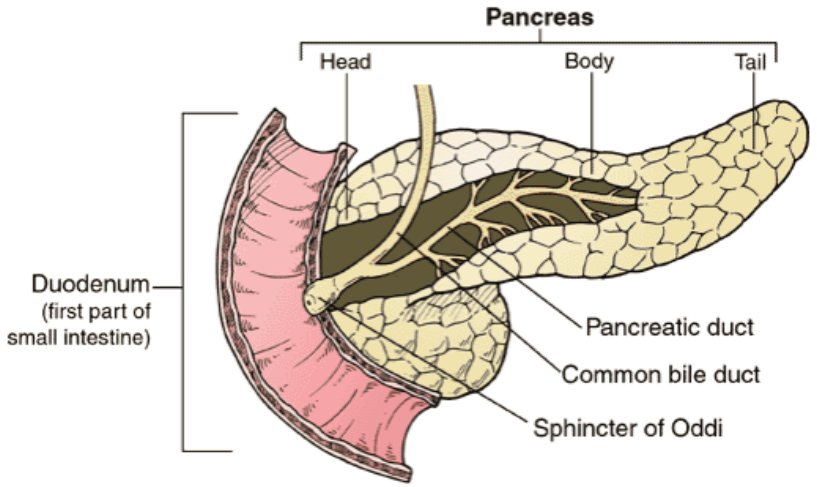
  - INSULIN

Insulin Is Secreted by the Pancreas In Proportion To Circulating Glucose Levels

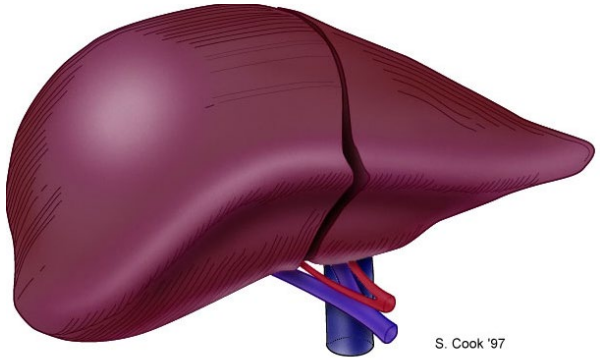
1. Blood insulin levels rise and fall in response to glucose excursions
2. Glucose is the key regulator of insulin secretion
3. ***Pancreatic β-cells "sense" a rise of glucose levels above 70 mg/dl***

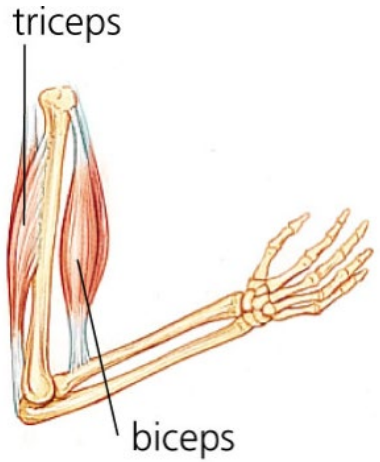


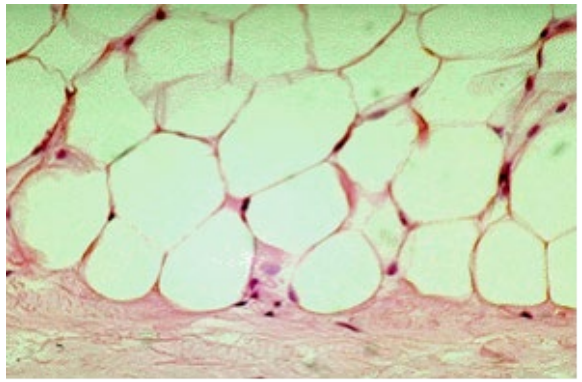
What does insulin do?



Slows glucose production by the liver



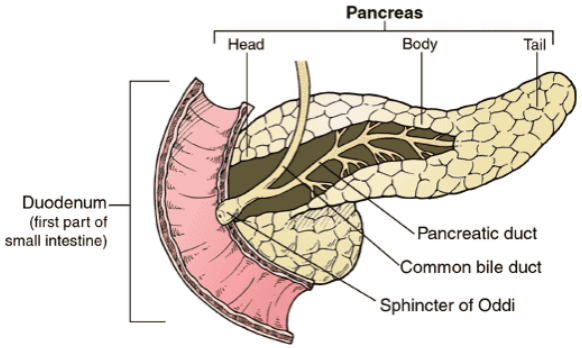


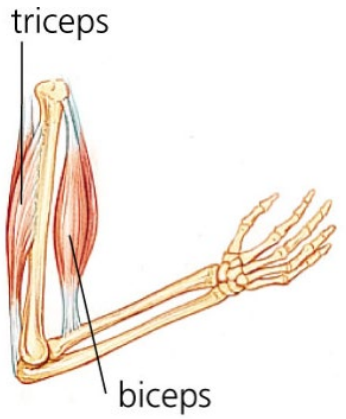


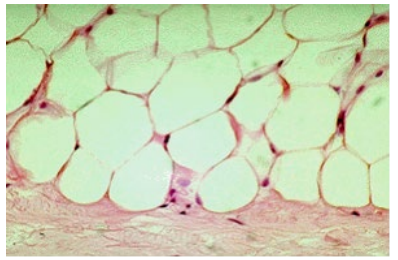
Stimulates glucose uptake into muscle and fat from the blood-stream

How does diabetes mellitus develop?

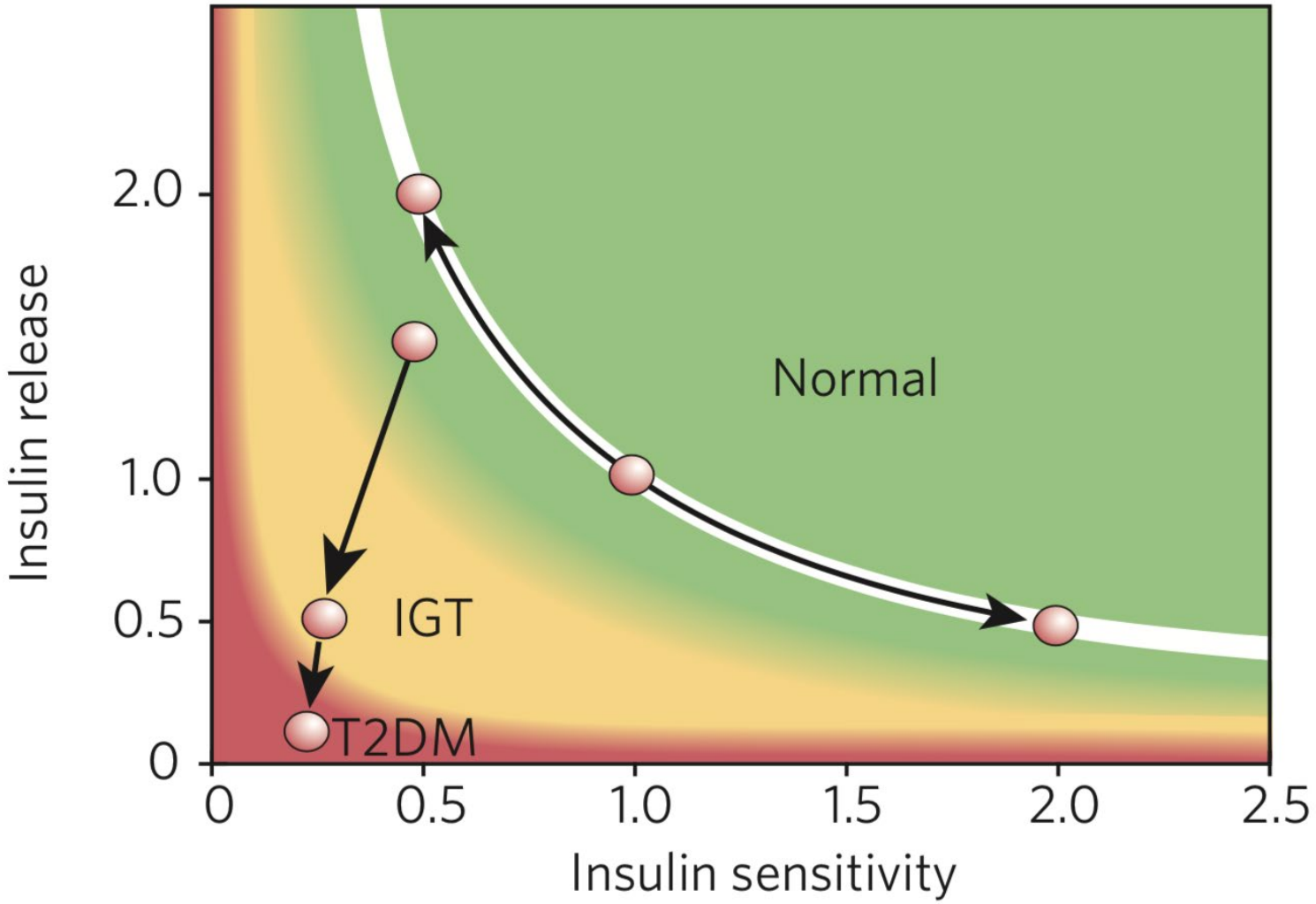
- Diabetes Mellitus occurs when there is an ABSOLUTE or RELATIVE deficiency of insulin, blood glucose levels remain elevated.
- Contributing factors:
  - **Progressive lack of function of the cells that make insulin (beta cells of the pancreas)**
  - Resistance to the effects of insulin







Normal Glucose Tolerance Is Maintained So Long As Insulin Release Is Adequate



How do we diagnose diabetes?

- If symptoms of DM are present: random plasma glucose concentration ≥ 200 mg/dl (≥ 11.1 mM) confirms the diagnosis of DM

- **Diabetes Mellitus, in the absence of symptoms**
  - FPG ≥ 126 mg/dl (≥7.0 mM)
  - *Hb A1C ≥ 6.5% (sometimes not accurate after organ transplant)*
  - Two-hour plasma glucose ≥ 200 mg/dl (≥ 11.1 mM) during an oral glucose tolerance test
  - In the absence of symptoms, a positive test must be confirmed on another day
  - It is unclear whether all of these criteria can be applied to children, all ethnic groups, or patients with certain disease states.

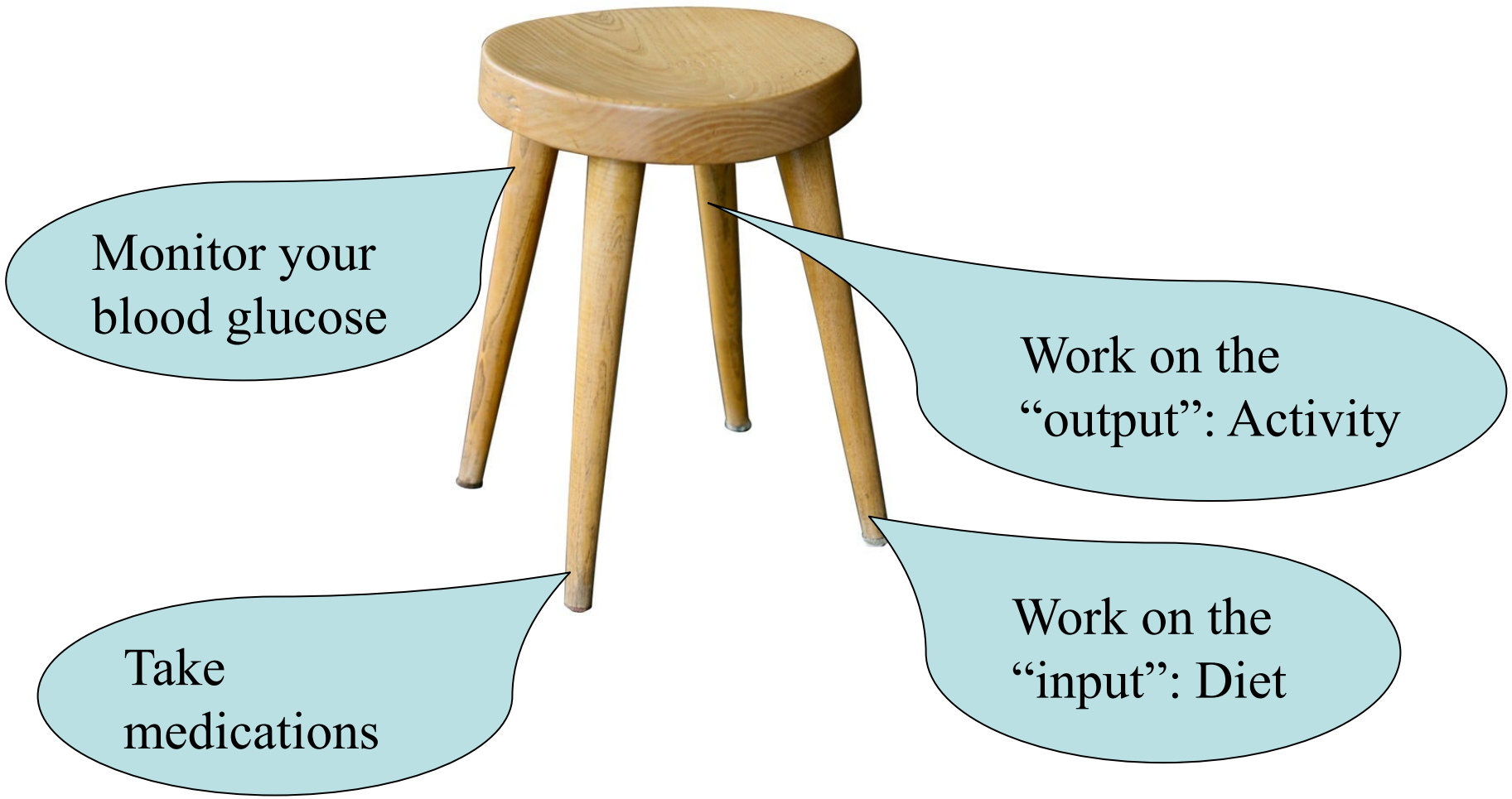
What factors during or after organ transplantation contribute to diabetes?

- “Steroids”/glucocorticoids/prednisone
  - Impairs insulin action, particularly after food intake
- Some immunosuppressant medications (tacrolimus, sirolimus)
  - Impair beta-cell function
  - Low magnesium levels
- Illness/inflammation/stress
  - Increased resistance to insulin in the tissues.

What are the consequences of diabetes mellitus?

- **Short-term: excessive urination, thirst, severe dehydration, stroke, maybe acid build up in the blood**
- **Medium-term: Cardiovascular disease, Risk of infection**
- Long-term:
  - damage to eyes, kidneys and nerves

How best to take care of diabetes?



How best to take care of diabetes?

Monitor blood glucose: Why, When, What

- Why?
  - Self-education
    - Bedtime and fasting: what happens when you don't eat
    - Pre-meal 2 hours post-meal: what happens when you eat
  - Adjust insulin dosages
- How often?
  - Depends on your medical regimen
- What are good numbers?
  - Fasting: 80-130 mg/dL
  - Pre-meal: 100-160 mg/dL

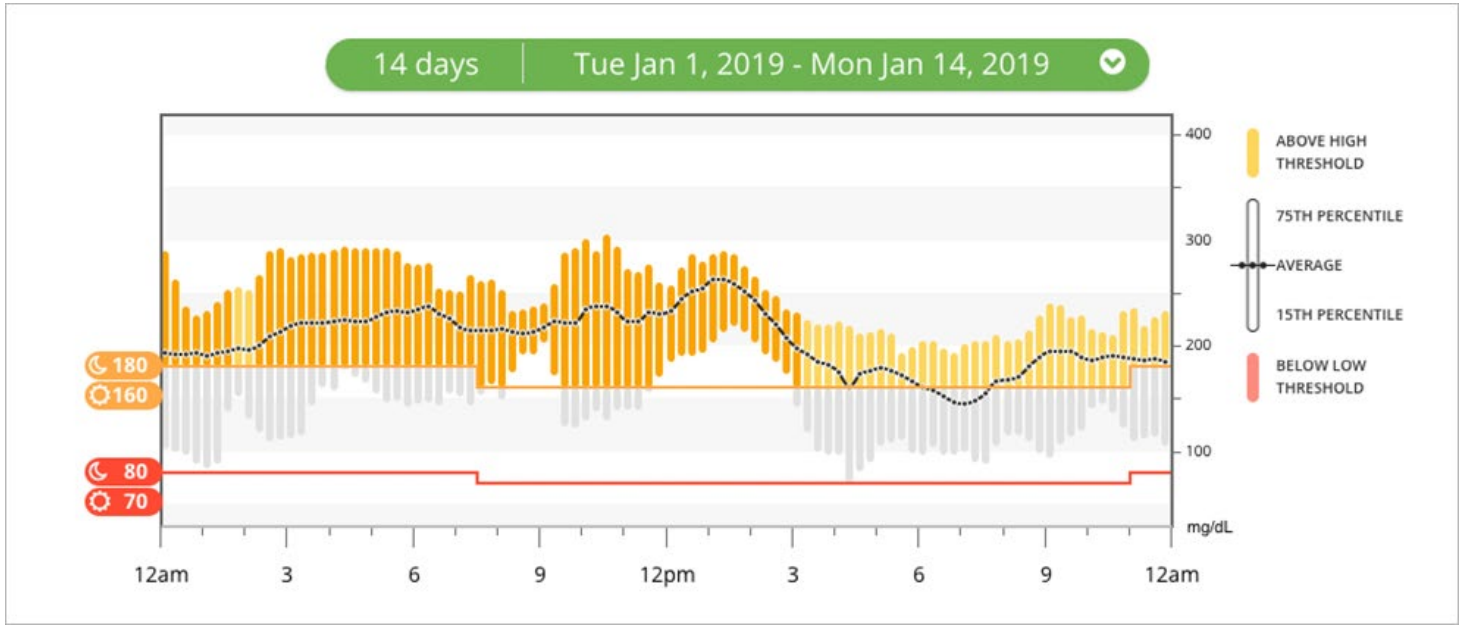
Monitor blood glucose Tools

Glucometer + Finger-stick: blood glucose

Continuous glucose monitors: close to blood glucose

Monitor blood glucose
Tools – a word about CGMs

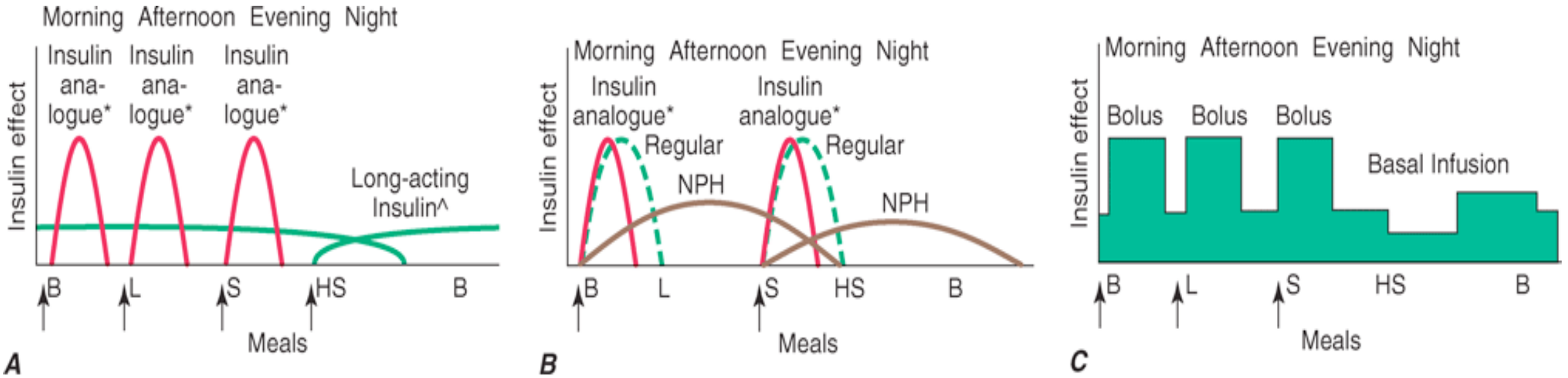
- Allows for detailed data review by providers and shared decision making
- Safety against hypoglycemia (low blood glucose)



Medications: Non-insulins

- Pills or injections
- Different modes of action:
  - Improve resistance to insulin
  - Improve beta-cell capacity
  - Reduce appetite
  - Increased urinary excretion of glucose
- Some newer medications (“flozins” and “glutides”) have not been well studied – need to be used with caution

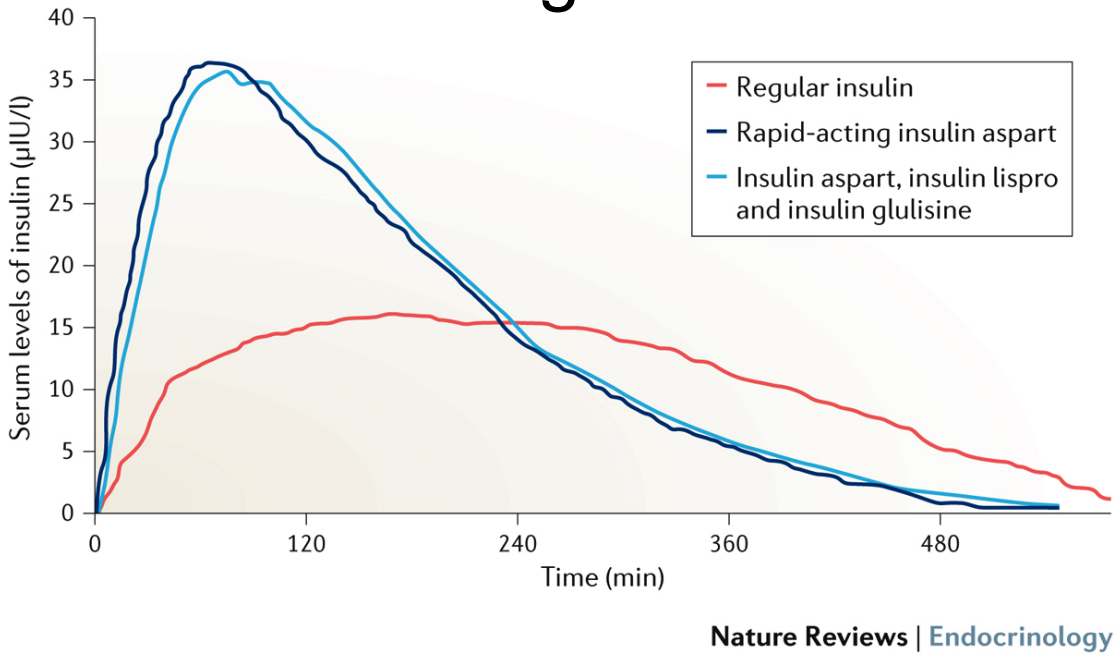
Medications: insulin based regimens



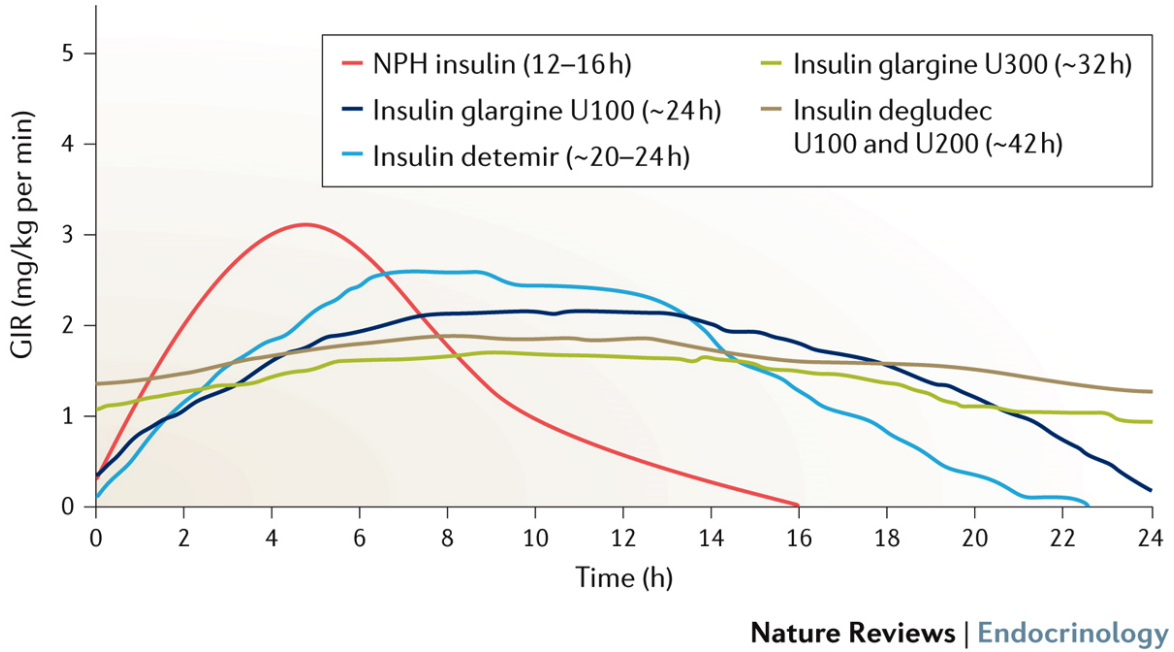
Source: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL, Loscalzo J: *Harrison's Principles of Internal Medicine, 18th Edition*: www.accessmedicine.com

Medications: insulin based regimens

Short-acting insulins



Intermediate/long-acting insulins



Caution regarding some treatments

- **HYPOGLYCEMIA**
  - Glucose less than 70 mg/dL is considered low
  - Below a glucose of 55 mg/dL, brain function may be compromised and risk for seizures, coma and death increases
  - Once you take a dose of insulin or sulfonylurea (glipizide, glimepiride), you can't take it back
  - Avoid glyburide
- Gastrointestinal side effects
- Dehydration

Lifestyle regimens

- Visiting with nutritionist to learn about diabetes and diet is critical
- Repeated visits help solidify and expand knowledge
- Many RDs also provide excellent education about diabetes and self-management skills
- Exercise: proceed as allowed by your transplant team
- Both strength and aerobic exercise have benefits
  - Be cautious about low glucoses after aerobic exercise in particular

Summary

- Diabetes occurs when there is an absolute or relative deficiency of insulin
- After transplant, steroids and calcineurin inhibitors in particular predispose to diabetes
- Dedicated testing for diabetes is strongly encouraged given high prevalence
- Treatment is needed to prevent complications
- Many different treatment modalities are available
- Some require vigilance for low blood glucose
- New tools have made monitoring glucose easier and contribute to increased safety

Thank you for this opportunity and for your attention!

Questions ?